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Compounds have potential for diagnosis, treatment of Alzheimer's disease

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New research suggests that a select group of compounds that interact with a protein in the brain might be used in the early diagnosis and treatment of Alzheimer's disease and other dementia disorders.

Scientists have discovered that these compounds interact in three specific ways with the tau protein, which is the subject of a growing body of research into the causes and progression of dementia.

In a normal, healthy brain, the tau protein binds to and stabilizes structures in the brain that are essential for proper functioning. But tau protein that breaks away from these structures can begin forming long strands called filaments. These filaments can clump into tangles, which are a marker of Alzheimer's disease and other neurodegenerative disorders.

Depending on the specific compounds under study, they can produce three different outcomes when introduced to the tau protein: They either bind to the protein filaments; inhibit the filaments from developing; or drive tau protein to form filaments. So far, the interactions have been observed in test tubes and cell cultures, so any clinical use of the compounds will require years of additional research.

All three interactions are expected to increase scientists' understanding of the neurodegenerative disease process, said Nicolette Honson, a postdoctoral researcher in the Center for Molecular Neurobiology at Ohio State University. But certain compounds seem to show potential to

allow for earlier diagnosis of Alzheimer's and other neurodegenerative disorders because of their tendency to seek out and stick to tau filaments, Honson said.

"It's important now to find compounds that can be used in imaging because the earlier clinicians can detect the disease, the better the chances are that a drug will halt disease progression while patients still have strong cognitive abilities," she said.

Honson described the research today (8/20) at the American Chemical Society meeting in Philadelphia.

Currently, images of the brain that can detect Alzheimer's disease use compounds designed to locate another marker of dementia: plaques of the peptide amyloid beta. Both these plaques and tangles are present in the brains of people with certain dementia disorders.

Researchers are engaged in a debate about whether the plaques and tangles are mere markers of disease or actually have a role in causing neurodegenerative diseases to progress. So far, they know the presence of tau tangles can occur in the human brain many years before any cognitive decline is apparent.

Alzheimer's disease is the most common form of dementia among older people. It initially involves the parts of the brain that control thought, memory and language. The cause is unknown and there is no cure. An estimated 4.5 million Americans suffer from Alzheimer's, according to the National Institute on Aging.

Honson and colleagues, led by Jeff Kuret, professor of molecular and cellular biochemistry at Ohio State, plan to test binding compounds on donated human brain tissue made available for research. The scientists will add the compounds to sections of brain tissue from Alzheimer's

disease patients and to healthy brain tissue to test whether the compounds continue to stick to tau tangles under the conditions present in a diseased brain.

Another family of compounds the researchers studied was able to stop tau from forming filaments, hinting at the compounds' potential as a basis for therapies to treat dementia diseases characterized by the formation of tau tangles.

"When we added these compounds to the reaction, their interaction with the tau protein inhibited filaments from forming, which could be valuable for therapeutics because it would prevent the formation of tau tangles. Some people think if we clear away the pathology seen in diseased brains, that might alleviate symptoms of Alzheimer's disease," Honson said.

These compounds will be tested in mice that have been genetically modified to have the characteristics of dementia to see if the compounds have similar inhibiting effects in an animal model.

A third finding of a family of compounds that can cause tau protein to form filaments will allow scientists to study the disease process. Honson noted that she and colleagues could induce filament formation with these compounds and then use that induced disease model to test the compounds that might be able to stop the disease from progressing.

Source: Ohio State University